Citation:

Ngandu T, Helkala EL, Soininen H, Winblad B, Tuomilehto J, Nissinen A, Kivipelto M. Alcohol drinking and cognitive functions: findings from the Cardiovascular Risk Factors Aging and Dementia (CAIDE) Study. *Dementia and Geriatric Cognitive Disorders.* 2007;23:140-149.

PubMed ID: 17170526

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To investigate whether alcohol drinking in midlife is associated with cognitive function later on in a nondemented population of elderly persons.

Inclusion Criteria:

- Participants of the Cardiovascular Risk Factors Aging and Dementia (CAIDE) study were derived from random population-based samples in two geographical areas in Eastern Finland.
- They were studied in 1972, 1977, 1982, or 1987 with the framework in North Karelia Project and FINMONICA Study.
- The population of the current study comprised 1,341 nondemented participants at follow-up.

Exclusion Criteria:

- Demented participants
- Missing information about alcohol intake

Description of Study Protocol:

Recruitment

- Participants of the CAIDE study were derived from random population-based samples in two geographical areas in Eastern Finland studied in 1972, 1977, 1982, and 1987 within the framework in North Karelia Project and FINMONICA Study.
- A random sample of 2,000 survivors aged 65-79 years in 1997 were invited for reexamination in 1998.
- 1,409 of these subjects completed reexamination.
- This study involved 1,341 nondemented participants (68 were excluded due to dementia) at

follow-up: 835 women and 506 men.

Design: Prospective cohort study

Survey methods used during baseline (midlife) visit were standardized following international recommendations. The survey included a self-administered questionnaire on health behavior, health status, medical history and socioeconomic status. Blood pressure, height, and weight were measured and a venous sample blood specimen was obtained. In 1998 the reexamination used the same survey methods and the ApoE genotype was determined and cognitive status assessed.

Participants were classified into three groups: those who never drank alcohol (never), those who drank less frequently than once per month (infrequent), and those who drank once per month or more often (frequent). The effect of change in drinking between midlife and late life was analyzed by grouping the persons in all nine possible categories. The effect of specific alcohol beverages was also analyzed.

All participants were given a battery of cognitive tests in the late-life examination. The Mini-Mental State Examination (MMSE) was administered to measure global cognitive function.

Blinding used (if applicable): Not noted by author.

Intervention (if applicable): Not applicable

Statistical Analysis

- Bivariate comparisons of the characteristics of the participants were done using X^2 test, t test, and analysis of variance.
- The effect of alcohol drinking on cognition; analysis of covariance models were used for all cognitive tests, with Bonferroni adjustments for multiple comparisons.
- Analyses were adjusted for age, sex, education, and follow-up time as well as for midlife vascular factors (systolic blood pressure, BMI, total cholesterol level, smoking status), ApoE4 carrier status, late-life history of myocardial infarction, stroke and diabetes, late-life living status, income level, and depressive symptoms.

Data Collection Summary:

Timing of Measurements

- Surveys were given at baseline (midlife) and at follow-up (average of 21 years, at ages 65-79 years)
- Survey methods used during baseline (midlife) visit were standardized following international recommendations. The survey included a self-administered questionnaire on health behavior, health status, medical history and socioeconomic status.
- Blood pressure, height, and weight were measured and a venous sample blood specimen was obtained.
- In 1998 the reexamination used the same survey methods and the ApoE genotype was determined and cognitive status assessed.

Dependent Variables

- Cognitive function: all participants were given a battery of cognitive tests in the late-life examination. The Mini-Mental State Examination (MMSE) was administered to measure

global cognitive function.

Independent Variables

- Alcohol intake at midlife defined as never, infrequent or frequent
- Participants were classified into three groups: those who never drank alcohol (never), those who drank less frequently than once per month (infrequent), and those who drank once per month or more often (frequent). The effect of change in drinking between midlife and late life was analyzed by grouping the persons in all nine possible categories. The effect of specific alcohol beverages was also analyzed.

Control Variables

- Age
- Sex
- Education
- Follow-up time
- Midlife vascular factors (systolic blood pressure, BMI, total cholesterol level, smoking status)
- ApoE4 carrier status
- Late-life history of myocardial infarction, stroke and diabetes
- Late-life living status
- Income level
- Depressive symptoms

Description of Actual Data Sample:

Initial N: 2,000

Attrition (final N): 1,341 participants [835 women (62.3%)].

Age: 65 - 79 years

Ethnicity: not reported

Other relevant demographics:

Anthropometrics

30% of the participants did not drink alcohol at the time of their midlife examination, 40% drank infrequently and 30% drank frequently. The never drinkers were older, less educated and more often women.

Smoking was more prevalent among frequent alcohol drinkers and among men.

In late life, never drinkers more often belonged to the lower income category and lived alone and had higher scores on the Beck Depression Inventory.

Location: Finland

Summary of Results:

Key Findings

- Participants who did not drink alcohol at mid-life had a poorer performance in episodic memory, psychomotor speed and executive function in late life compared with infrequent and frequent drinkers, adjusted for sociodemographic and vascular factors.
- Late-life drinkers had poorer psychomotor speed and executive function.

Other Findings

- No interactions between apolipoprotein E4 and alcohol or sex and alcohol were found.

Cognitive Functioning in Late Life in Relation to the Midlife and Late-Life Drinking Frequency (sample 1972/1977).

	Mid-life alcohol drinking				Late-life alcohol drinking			
Variables	never	infrequent	frequent	p^1, p^2	never	infrequent	frequent	p^1,p^2,p^3
	n=285	n=403	n=278		n=265	n=326	n=363	
Global cognitive functioning	26.0 (0.1)	26.2(0.1)	26.3(0.1)		26.0(0.1)	26.0(0.1)	26.3(0.1)	
Episodic memory	4.9(0.1)	5.2(0.1)	5.2(0.1)	p^1=0.02 p^2=0.04	4.9(0.1)	5.0(0.1)	5.2(0.1)	p^2=0.02 p^3=0.06
Semantic memory	19.7(0.4)	20.9(0.3)	20.7(0.4)	p^1=0.08	20.4(0.4)	20.4(0.4)	21.0(0.4)	
Subjective memory	2.1(0.0)	2.1(0.0)	2.1(0.0)		2.1(0.0)	2.1(0.0)	2.1(0.0)	
Prospective memory	2.6(0.1)	2.8(0.0)	2.8(0.1)	p^2=0.05	2.6(0.1)	2.7(0.1)	2.9(0.0)	p^2=0.01 p^3=0.02
Executive function	44.0(1.4)	37.2(1.1)	38.1(1.4)	p^1=0.00 p^2=0.01	43.0(1.5)	37.8(1.2)	38.5(1.2)	p^1=0.02 p^2=0.06
Psychomotor speed	-0.04(0.1)	0.19(0.0)	0.19(0.0)	p^1=0.00 p^2=0.01	-0.02(0.1)	0.14(0.1)	0.20(0.0)	p^1=0.06 p^2=0.01

p^1=difference between never and infrequent

p^2=difference between never and frequent

p^3=difference between infrequent and frequent

Author Conclusion:

Nondrinkers had a poorer cognitive performance than drinkers, especially in the domains related to fluid intelligence (executive function, psychomotor speed, and episodic memory). Other cognitive functions showed little associations with alcohol drinking. It is not clear whether the association is causal,nor are the mechanisms involved understood. The safe limit for drinking for the best

cognitive function remains unknown.

Reviewer Comments:

Strengths of the research:

- *Population-based data with high participation rate*
- *Information on alcohol intake was included both midlife and late life intake.*
- *The change in drinking frequency was also able to be associated with cognitive function.*
- *Data on several domains of cognitive function was available.*

Limitations of the research:

- *Analyses were based on self-reporting of intake.*
- *At the midlife assessment it was assumed that most of the subjects were cognitively intact.*
- *There was insufficient power for the subanalyses of alcohol specific differences, ApoE4 carriers.*
- *Differences between test results between groups with best and poorest performance were not large.*
- *Other social and lifestyle-related factors that are associated with drinking and cognitive ability may impact outcome.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes

2.	**Was the selection of study subjects/patients free from bias?**	???
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	???
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	???
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	No
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	???

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	???
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	???
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		???
	10.1.	Were sources of funding and investigators' affiliations described?	???
	10.2.	Was the study free from apparent conflict of interest?	???